IFNβ G162C-Ig direct fusion construct open reading frame

```
   1 ATGCCTGGGAAGATGGTCGTGATCCTTGGAGCCTCAAATATACTTTGGATAATGTTTGCA  60
     M  P  G  K  M  M  V  V  I  L  L  G  A  S  N  I  L  W  I  M  F  A

  61 GCTTCTCAAGCCATGAGCTACAACTTGCTTGGATTCCTACAAAGAAGCAGCAATTTTCAG 120
     A  S  Q  A  M  S  Y  N  L  L  G  F  L  Q  R  S  S  N  F  Q

 121 TGTCAGAAGCTCCTGTGGCAATTGAATGGGAGGCTTGAATACTGCCTCAAGGACAGGATG 180
     C  Q  K  L  L  W  Q  L  N  G  R  L  E  Y  C  L  K  D  R  M

 181 AACTTTGACATCCCTGAGGAGATTAAGCAGCTGCAGCAGTTCCAGAAGGAGGACGCCGCA 240
     N  F  D  I  P  E  E  I  K  Q  L  Q  Q  F  Q  K  E  D  A  A

 241 TTGACCATCTATGAGATGCTCCAGAACATCTTTGCTATTTTCAGACAAGATTCATCTAGC 300
     L  T  I  Y  E  M  L  Q  N  I  F  A  I  F  R  Q  D  S  S  S

 301 ACTGGCTGGAATGAGACTATTGTTGAGAACCTCCTGGCTAATGTCTATCATCAGATAAAC 360
     T  G  W  N  E  T  I  V  E  N  L  L  A  N  V  Y  H  Q  I  N

 361 CATCTGAAGACAGTCCTGGAAGAAAAACTGGAGAAAGAGATTTCACCAGGGGAAAACTC 420
     H  L  K  T  V  L  E  E  K  L  E  K  E  D  F  T  R  G  K  L

 421 ATGAGCAGTCTGCACCTGAAAGATTATTATGGGAGGATTCTGCATTACCTGAAGGCCAAG 480
     M  S  S  L  H  L  K  R  Y  Y  G  R  I  L  H  Y  L  K  A  K
```

FIG. 1 A

BEST AVAILABLE COPY

```
481 GAGTACAGTCACTGTGCCTGGACCATAGTCAGAGTGGAAATCCTAAGGAACTTTTACTTC 540
      E  Y  S  H  C  A  W  T  I  V  R  V  E  I  L  R  N  F  Y  F

541 ATTAACAGACTTACATGTTACCTCCGAAACGTCGACAAAACTCACACATGCCCACCGTGC 600
      I  N  R  L  T  C  Y  L  R  N  V  D  K  T  H  T  C  P  P  C

601 CCAGCACCTGAACTCCTGGGGGGACCGTCAGTCTTCCTCTTCCCCCCAAAACCCAAGGAC 660
      P  A  P  E  L  L  G  G  P  S  V  F  L  F  P  P  K  P  K  D

661 ACCCTCATGATCTCCCGGACCCCTGAGGTCACATGCGTGGTGGTGGACGTGAGCCACGAA 720
      T  L  M  I  S  R  T  P  E  V  T  C  V  V  V  D  V  S  H  E

721 GACCCTGAGGTCAAGTTCAACTGGTACGTGGACGGCGTGGAGGTGCATAATGCCAAGACA 780
      D  P  E  V  K  F  N  W  Y  V  D  G  V  E  V  H  N  A  K  T

781 AAGCCGCGGGAGGAGCAGTACAACAGCACGTACCGTGTGGTCAGCGTCCTCACCGTCCTG 840
      K  P  R  E  E  Q  Y  N  S  T  Y  R  V  V  S  V  L  T  V  L

841 CACCAGGACTGGCTGAATGGCAAGGAGTACAAGTGCAAGGTCTCCAACAAAGCCCTCCCA 900
      H  Q  D  W  L  N  G  K  E  Y  K  C  K  V  S  N  K  A  L  P

901 GCCCCCATCGAGAAAACCATCTCCAAAGCCAAAGGGCAGCCCCGAGAACCACAGGTGTAC 960
      A  P  I  E  K  T  I  S  K  A  K  G  Q  P  R  E  P  Q  V  Y
```

FIG. 1 B

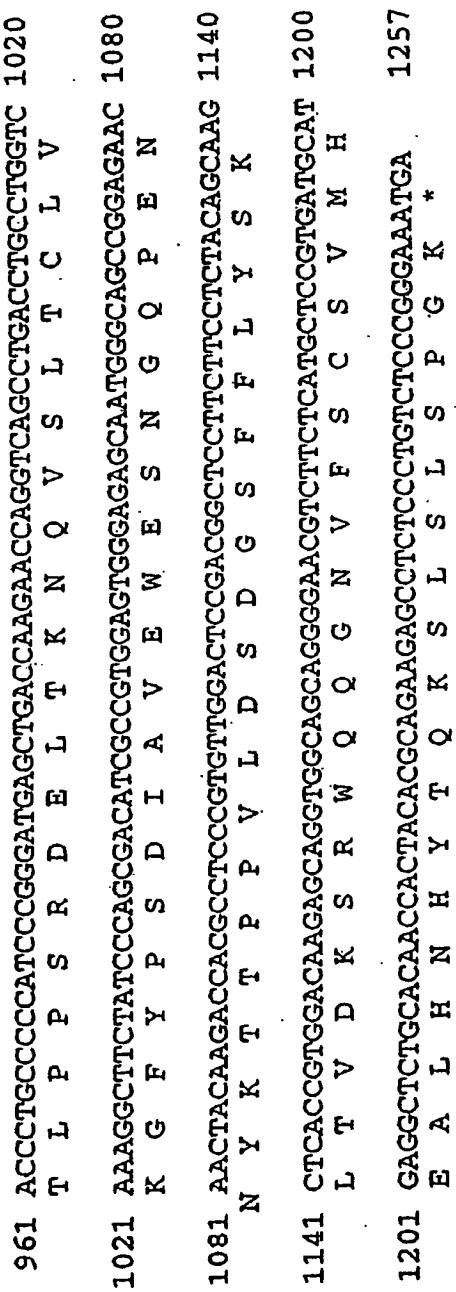

961 ACCCTGCCCCCCATCCCGGGATGAGCTGACCAAGAACCAGGTCAGCCTGACCTGCCTGGTC 1020
T L P P S R D E L T K N Q V S L T C L V
1021 AAAGGCTTCTATCCCAGCGACATCGCCGTGGAGTGGGAGAGCAATGGGCAGCCGGAGAAC 1080
K G F Y P S D I A V E W E S N G Q P E N
1081 AACTACAAGACCACGCCTCCCGTGTTGGACTCCGACGGCTCCTTCTTCCTCTACAGCAAG 1140
N Y K T T P P V L D S D G S F F L Y S K
1141 CTCACCGTGGACAAGAGCAGGTGGCAGCAGGGGAACGTCTTCTCATGCTCCGTGATGCAT 1200
L T V D K S R W Q Q G N V F S C S V M H
1201 GAGGCTCTGCACAACCACTACACGCAGAAGAGCCTCTCCCTGTCTCCCGGGAAATGA 1257
E A L H N H Y T Q K S L S L S P G K *

FIG. 1 C

IFNβ G162C-Ig fusion G4S linker construct open reading frame

```
   1 ATGCCTGGGAAGATGGTCGTGATCCTTGGAGCCTCAAATATACTTTGGATAATGTTTGCA 60
     M  P  G  K  M  M  V  V  I  L  L  G  A  S  N  I  L  W  I  M  F  A

  61 GCTTCTCAAGCCATGAGCTACAACTTGCTTGGATTCCTACAAAGAAGCAGCAATTTTCAG 120
     A  S  Q  A  M  S  Y  N  L  L  G  F  L  Q  R  S  S  N  F  Q

 121 TGTCAGAAGCTCCTGTGGCAATTGAATGGGAGGCTTGAATACTGCCTCAAGGACAGGATG 180
     C  Q  K  L  L  W  Q  L  N  G  R  L  E  Y  C  L  K  D  R  M

 181 AACTTTGACATCCCTGAGGAGATTAAGCAGCTGCAGCAGTTCCAGAAGGAGGACGCCGCA 240
     N  F  D  I  P  E  E  I  K  Q  L  Q  Q  F  Q  K  E  D  A  A

 241 TTGACCATCTATGAGATGCTCCAGAACATCTTTGCTATTTTCAGACAAGATTCATCTAGC 300
     L  T  I  Y  E  M  L  Q  N  I  F  A  I  F  R  Q  D  S  S  S

 301 ACTGGCTGGAATGAGACTATTGTTGAGAACCTCCTGGCTAATGTCTATCATCAGATAAAC 360
     T  G  W  N  E  T  I  V  E  N  L  L  A  N  V  Y  H  Q  I  N

 361 CATCTGAAGACAGTCCTGGAAGAAAACTGGAGAAGATTTCACCAGGGGAAAACTC 420
     H  L  K  T  V  L  E  E  K  L  E  K  E  D  F  T  R  G  K  L
```

FIG. 2A

```
421 ATGAGCAGTCTGCACCTGAAAAGATATTATGGAGGATTCTGCATTACCTGAAGGCCAAG 480
    M  S  S  L  H  L  K  K  R  R  Y  Y  Y  G  G  R  I  L  L  H  Y  Y  L  K  A  K

481 GAGTACAGTCACTGTGCCTGGACCATAGTCAGAGTGGAAATCCTAAGGAACTTTTACTTC 540
    E  Y  S  H  C  A  W  T  I  I  V  R  R  V  E  I  L  R  N  F  Y  Y  F

541 ATTAACAGACTTACATGTTACCTCCGAAACGGCGGTGGTGGCAGCGTCGACAAAACTCAC 600
    I  N  R  L  T  C  Y  L  R  N  G  G  G  G  S  V  D  K  T  H

601 ACATGCCCACCGTGCCCAGCACCTGAACTCCTGGGGGGACCGTCAGTCTTCCTCTTCCCC 660
    T  C  P  P  C  P  A  P  E  L  L  G  G  P  S  V  F  L  F  P

661 CCAAAACCCAAGGACACCCTCATGATCTCCCGGACCCCTGAGGTCACATGCGTGGTGGTG 720
    P  K  P  K  D  T  L  M  I  S  R  T  P  E  V  T  C  V  V  V

721 GACGTGAGCCACGAAGACCCTGAGGTCAAGTTCAACTGGTACGTGGACGGCGTGGAGGTG 780
    D  V  S  H  E  D  P  E  V  K  F  N  W  Y  V  D  G  V  E  V

781 CATAATGCCAAGACAAAGCCGCGGGAGGAGCAGTACAACAGCACGTACCGTGTGGTCAGC 840
    H  N  A  K  T  K  P  R  E  E  Q  Y  N  S  T  Y  R  V  V  S

841 GTCCTCACCGTCCTGCACCAGGACTGGCTGAATGGCAAGGAGTACAAGTGCAAGGTCTCC 900
    V  L  T  V  L  H  Q  D  W  L  N  G  K  E  Y  K  C  K  V  S

901 AACAAAGCCCTCCCAGCCCCCATCGAGAAAACCATCTCCAAAGCCAAAGGGCAGCCCCGA 960
    N  K  A  L  P  A  P  I  E  K  T  I  S  K  A  K  G  Q  P  R
```

FIG. 2B

```
961 GAACCACAGGTGTACACCCTGCCCCCATCCCGGGATGAGCTGACCAAGAACCAGGTCAGC 1020
      E  P  Q  V  Y  T  L  P  P  S  R  D  E  L  T  K  N  Q  V  S

1021 CTGACCTGCCTGGTCAAAGGCTTCTATCCCAGCGACATCGCCGTGGAGTGGGAGAGCAAT 1080
      L  T  C  L  V  K  G  F  Y  P  S  D  I  A  V  E  W  E  S  N

1081 GGGCAGCCGGAGAACAACTACAAGACCACGCCTCCCGTGTTGGACTCCGACGGCTCCTTC 1140
      G  Q  P  E  N  N  Y  K  T  T  P  P  V  L  D  S  D  G  S  F

1141 TTCCTCTACAGCAAGCTCACCGTGGACAAGAGCAGGTGGCAGCAGGGGAACGTCTTCTCA 1200
      F  L  Y  S  K  L  T  V  D  K  S  R  W  Q  Q  G  N  V  F  S

1201 TGCTCCGTGATGCATGAGGCTCTGCACAACCACTACACGCAGAAGAGCCTCTCCCTGTCT 1260
      C  S  V  M  H  E  A  L  H  N  H  Y  T  Q  K  S  L  S  L  S

1261 CCCGGGAAATGA 1272
      P  G  K  *
```

FIG. 2C

FIG. 3

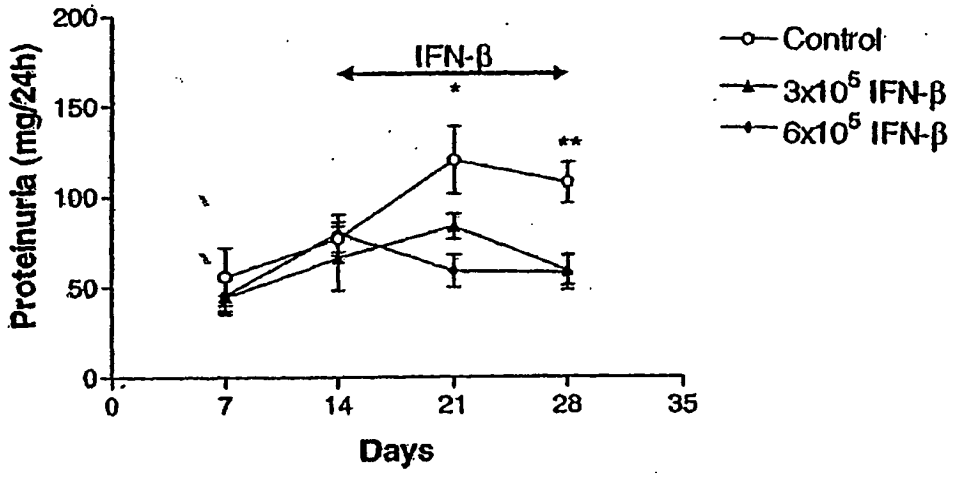

Proteinuria (mg/24h)
200
150
100
50
0
IFN-β
*
**
0
7
14
21
28
35
Days
Control
3x10^5 IFN-β
6x10^5 IFN-β

FIG. 4

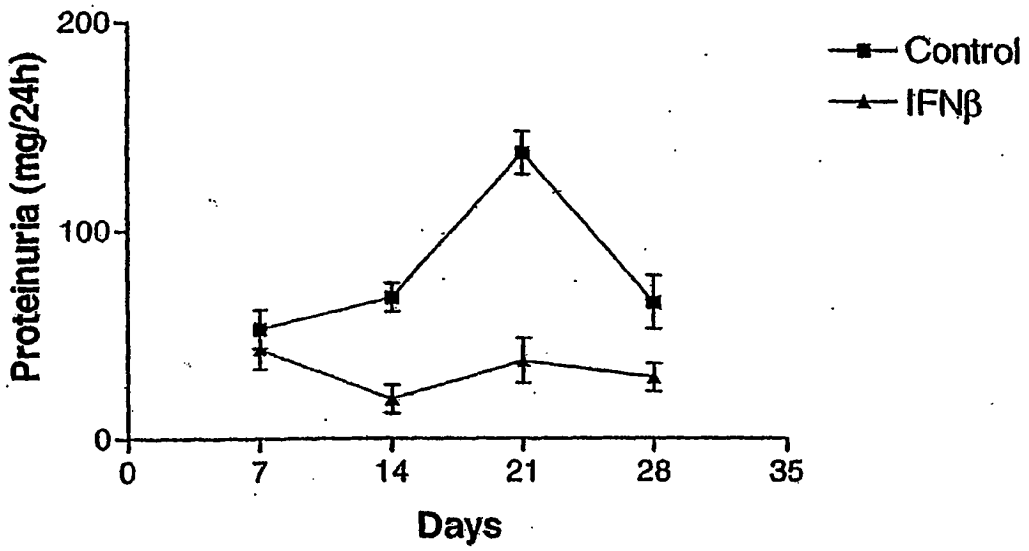


FIG. 5

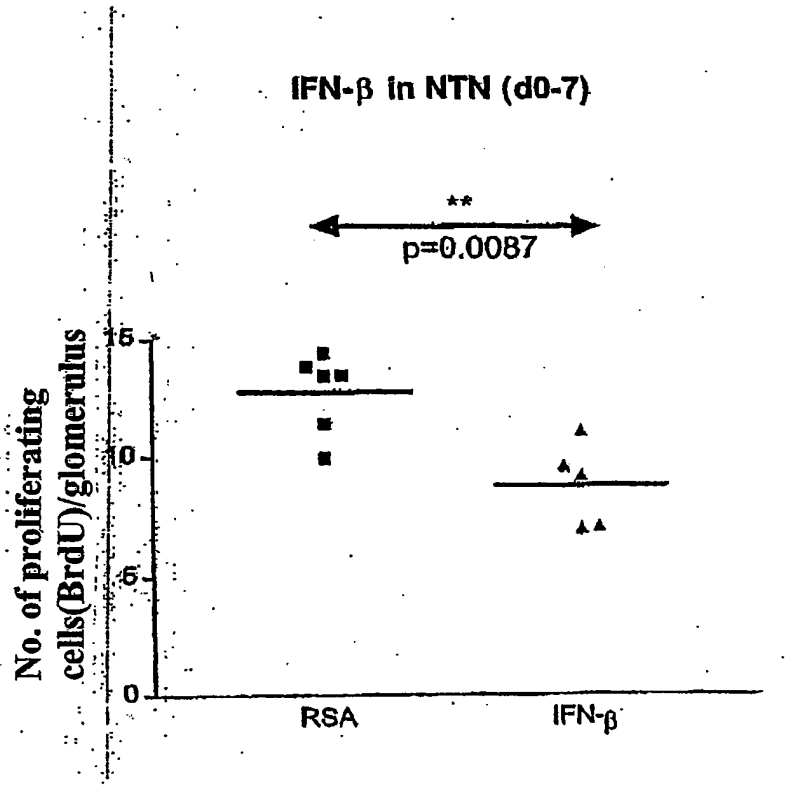

IFN-β in NTN (d0-7)
**
p=0.0087
No. of proliferating cells(BrdU)/glomerulus
15
10
5
0
RSA
IFN-β

FIG. 6

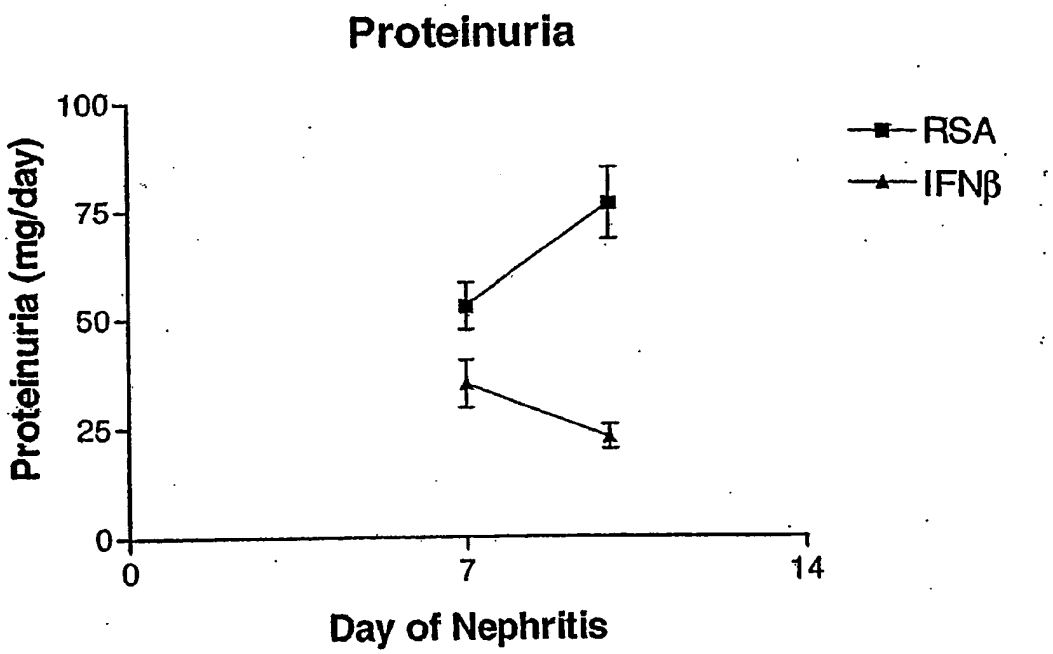

Proteinuria
Proteinuria (mg/day)
100
75
50
25
0
0
7
14
Day of Nephritis
RSA
IFNβ

FIG. 7

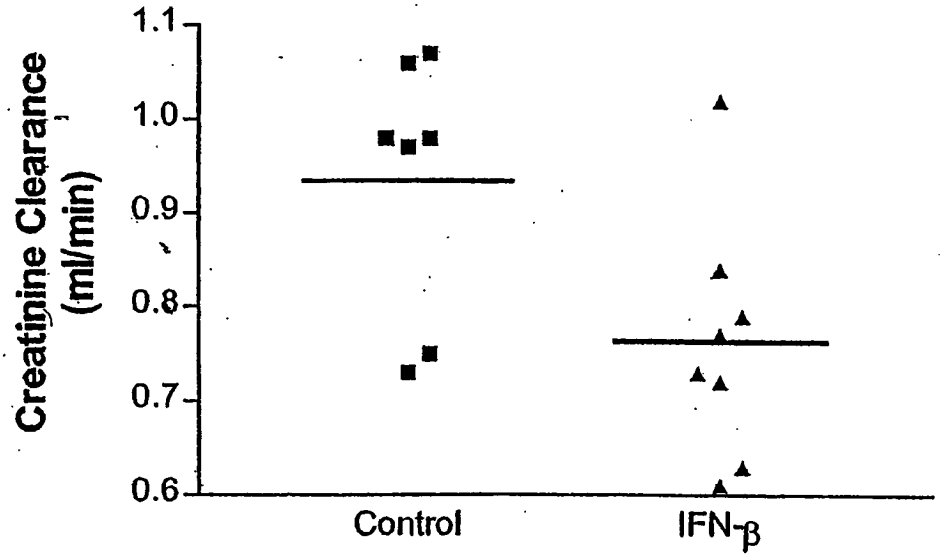


FIG. 8

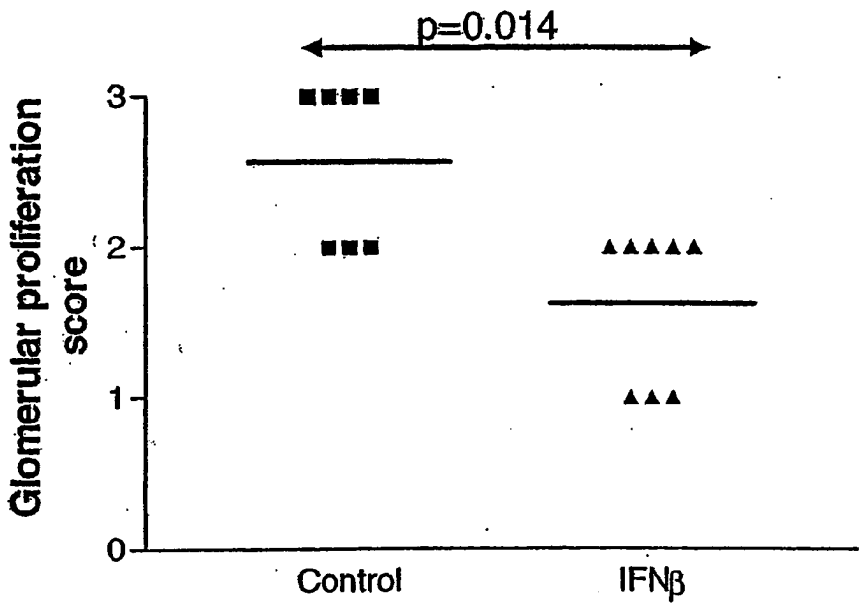
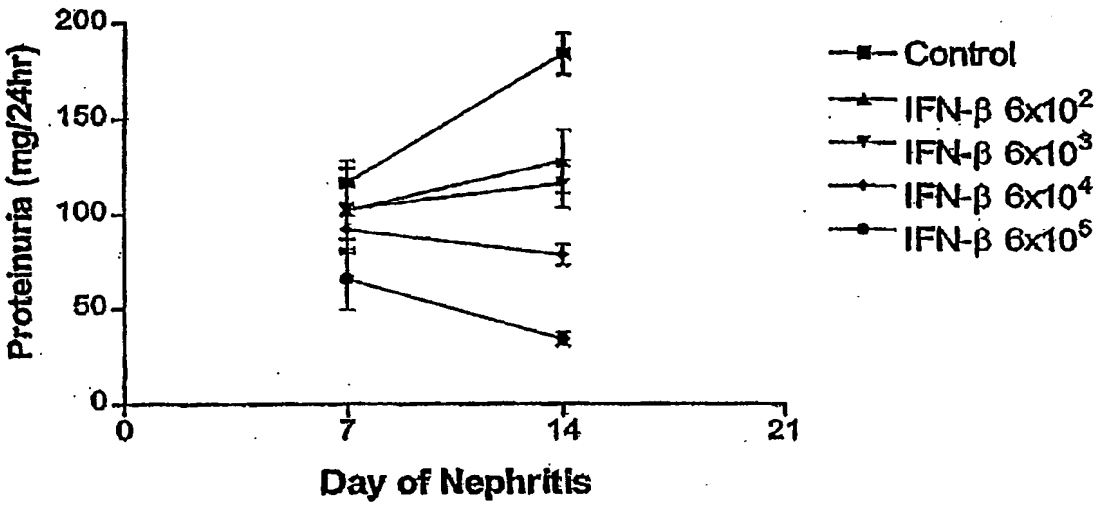


FIG. 9


Proteinuria (mg/24hr)
200
150
100
50
0
0
7
14
21
Day of Nephritis
Control
IFN-β 6x10²
IFN-β 6x10³
IFN-β 6x10⁴
IFN-β 6x10⁵

This Page is Inserted by IFW Indexing and Scanning Operations and is not part of the Official Record

BEST AVAILABLE IMAGES

Defective images within this document are accurate representations of the original documents submitted by the applicant.

Defects in the images include but are not limited to the items checked:

- ☐ BLACK BORDERS
- ☐ IMAGE CUT OFF AT TOP, BOTTOM OR SIDES
- ☑ FADED TEXT OR DRAWING
- ☐ BLURRED OR ILLEGIBLE TEXT OR DRAWING
- ☐ SKEWED/SLANTED IMAGES
- ☐ COLOR OR BLACK AND WHITE PHOTOGRAPHS
- ☐ GRAY SCALE DOCUMENTS
- ☑ LINES OR MARKS ON ORIGINAL DOCUMENT
- ☑ REFERENCE(S) OR EXHIBIT(S) SUBMITTED ARE POOR QUALITY
- ☐ OTHER: _____

IMAGES ARE BEST AVAILABLE COPY.

As rescanning these documents will not correct the image problems checked, please do not report these problems to the IFW Image Problem Mailbox.